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(54) Title: IMPROVED BONE MATRIX COMPOSITIONS AND METHODS

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(57) **Abstract:** The present invention provides methods of improving the osteogenic and/or chondrogenic activity of a bone matrix, e.g., a demineralized bone matrix (DBM), by exposing the bone matrix to one or more treatments or conditions. In preferred embodiments the bone matrix is derived from human bone. The treatment or condition may alter the structure of the bone matrix and/or cleave one or more specific proteins. Cleavage may generate peptides or protein fragments that have osteoinductive, osteogenic, or chondrogenic activity. Preferred treatments include collagenase and various other proteases. The invention further provides improved bone and cartilage matrix compositions that have been prepared according to the inventive methods and methods of treatment using the compositions. The invention further provides methods of preparing, testing, and using the improved bone matrix compositions. One assay comprises exposing relatively undifferentiated mesenchymal cells to a bone matrix composition and measuring expression of a marker characteristic of osteoblast or chondrocyte lineage(s). Increased expression of the marker relative to the level of the marker in cells that have been exposed to a control matrix (e.g., an inactivated or untreated matrix) indicates that the treatment or condition increased the osteogenic and/or chondrogenic activity of the bone matrix. Suitable cells include C2C12 cells. A suitable marker is alkaline phosphatase. The inventive methods increase the osteogenic and/or chondrogenic activity of human DBM when tested using this assay system.